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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/023,533	12/17/2001	Danping Li	LA0061 NP	5618

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 04/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/023,533	LI ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-16* is/are pending in the application.

4a) Of the above claim(s) *4-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 11-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Acknowledgement is made of applicants' filing of the instant application as a Request for Continued Examination (RCE) under 37 CFR 1.1114.

2. By Amendment filed December 13, 2004, claims 1 and 11-16 have been amended and claims 2-3 have been cancelled. Claims 1 and 4-16 are pending in the application, but claims 1 and 11-16 are currently being prosecuted on the merits since claims 4-10 are withdrawn from consideration as being directed to a non-elected invention.

New Matter

3. The amendment filed December 13, 2004 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: "being devoid of an enteric coating".

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1 and 11-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amendment filed February 23, 2004 introduces new claim limitation (negative limitation) into the claim 1. The amendment recites that said composition is "being devoid of an enteric coating".

The instant specification discloses that the pharmaceutical compositions of the present invention includes a combination of metformin and glipizide in a single formulation, wherein the glipizide content is uniform, and which formulation controls moisture so that the glipizide does not hydrolyze, yet the metformin is compressable; and wherein the metformin and glipizide are formulate together in a bilayered tablet which includes a first layer and a second layer (page 7, line 18 thru page 8, line 16). The specification states that the bilayered tablet of the invention may include an outer protective coating or finishing layer. As the specific embodiments of the outer protective coating or finishing layer of the tablet, the enteric coating is illustrated throughout the specification (page 8, lines 32-36; page 9, lines 1-18; page 16, line 1 thru page 17, 12).

The instantly recited "said composition being devoid of an enteric coating" completely excludes any possibility of having "enteric coating" on the outer surface of the single dosage formulation (e.g., tablet). There is no support in the specification for such negative limitation made by the presently claimed invention. Apparently, the applicant's amendment to overcome the rejection of the claims under 35 USC 102(b) as being anticipated by Chen et al. (US 6099862) introduces new matter into the claim.

Vas-Cath Inc. Mahurkar, 19 USPQ2d 1111, makes clear the "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966(1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989)* ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.*

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1 and 11-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al. (US 6099862) in view of Patel et al. (US 6248363 B1) and Bonhomme et al. (US 6303146).

Chen teaches a pharmaceutical tablet containing combination of metformin and glipizide, wherein core of said composition is prepared by mixing metformin and glipizide with povidone, sodium lauryl sulfate and magnesium stearate and then tablet is optionally seal coated with an opadry materals. As specific embodiments of the claimed invention, Examples (1-2) discloses 850mg or 500mg of metformin HCl and 5 mg of glipizide controlled release tablet, wherein

granules containing metformin and glipizide are dried "in the fluidized bed coater until the loss on drying is less than 2%" and then compressed to tablet.

Patel is being supplied as a reference to demonstrate the routine knowledge in art in preparing pharmaceutical actives such as metformin and glipizide in various pharmaceutical delivery systems including various dosage forms (e.g., tablet, capsule, quick or fast dissolving tablet, granule, etc...); coated with various coating methods (e.g., enteric coating, seal coating, protected coating or layered coating, etc...); and dosage form release system (e.g., immediate release, pulsatile release, controlled release, extended release, delayed release, targeted release). See column 6, line 32; column 7, line 7; column 9, line 3 and 66; column 10, line 31; column 41, line 29 thru column 51, line 10.

Bonhomme is being supplied as a reference to demonstrate the routine knowledge in art in determining 2-3% w/w moisture content prior to "tableting" (column 6, lines 37-49).

The teaching of Chen differs from the claimed invention in " being devoid of an enteric coating"; "2 to 3% by weight moisture"; and the specific dosage amounts of metformin and glipizide in said composition. However, it would have been obvious in view of Patel (US 6248363 B1) who teaches pharmaceutical delivery systems for pharmaceutical active ingredients including metformin and glipizide, wherein said active ingredients can be prepared in various dosage forms (e.g., tablet, capsule, quick or fast dissolving tablet, granule, etc...); coated with various coating methods (e.g., enteric coating, seal coating, protected coating or layered coating, etc...); and dosage form release system (e.g., immediate release, pulsatile release, controlled

release, extended release, delayed release, targeted release), and Bonhomme who teaches the routine knowledge in art in determining 2-3% w/w moisture content prior to "tableting".

The above references in combination make clear that the combination of metformin and glipizide in single dosage formulation is old and well known in the art. The above references in combination also make clear that the preparation of pharmaceutical composition containing metformin and/or glipizide in various dosage forms (e.g., tablet, quick, fast dissolving tablet, capsule, etc...) coated with coating techniques (e.g., enteric coating, protective coating, seal coating, etc...) designed for various dosage form release systems (e.g., immediate release, controlled release, delayed release, etc...) is old and well known in the art. Furthermore, the above references in combination make clear that optimization of "less than 2%" to "2 to 3% moisture" is well within the skill of the artisan. One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

With respect to the instantly required "devoid of an enteric coating", Patel teaches that determination of appropriate dosage forms (e.g., tablet covered with enteric coating or with protective coating or finishing layer) having optimum therapeutic index is well considered within the skill of the artisan, ant the artisan would be motivated to determine optimum dosage forms to maximize the effects of the drug. Therefore, the references in combination make obvious the claimed invention.

With respect to the specific dosage amounts of active ingredients in said composition, those of ordinary skill in the art readily optimize effective dosages as determined by good

medical practice and the clinical condition of the individual patient. Regardless of the manner of administration, the specific dose may be calculated according to body weight, body surface area or organ size. Further refinement of the calculations necessary to determine the appropriate dosage for treatment involving each of the above mentioned formulations is routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation, especially in light of the dosage information in column 5, lines 1-15.

Response to Arguments

6. Applicant's arguments filed December 13, 2004 have been fully considered but they are not persuasive.

Applicant's argument takes position that applicant's tablets are devoid of an enteric coating and therefore are immediate release tablets. Applicant alleges that the Chen's sustained release tablets differ from the instantly claimed immediate release tablets.

Unlike applicant's assertion, there is no indication in the present claims, however that said composition must be in the form of immediate release tablets. Applicant's recitation of "being devoid of an enteric coating" does not render the claimed composition to be essentially in the form of immediate release tablet. Since the interpretation of "being devoid of an enteric coating" means other types of known coating techniques of pharmaceutical compositions (e.g., seal coating, film coatings, barrier coatings, compress coatings, fast disintegrating coatings, or enzyme degradable coatings) designed for diverse dosage delivery forms, for example immediate release, pulsatile release, controlled release, extended release, delayed release, targeted release,

synchronized release, or targeted delayed release (see column 41, lines 55-63 of US 6248363), Chen's formulation makes obvious the claimed invention.

Even if applicant's argument is found persuasive, determination of appropriate dosage forms (e.g., tablet covered with enteric coating or with protective coating or finishing layer) having optimum therapeutic index is well considered within the skill of the artisan as evidenced by Patel et al. (US 6248363).

Applicant's argument takes position that there is no disclosure or suggestion in Chen et al. of "2 to 3% moisture" of tablet. The examiner agrees. Chen discloses that the granules containing metformin and glipizide are "dried in the fluidized bed coater until the loss on drying is less than 2%" prior to "tableting". Although Chen's formulation containing "less than 2%" of moisture differs from the instantly required concentration of "2 to 3% moisture", the examiner considers that such determination is well within the skill of the artisan as evidenced by Bonhomme,

Conclusion

7. No Claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (703) 872-9306.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Brian Kwon
Patent Examiner
AU 1614